

IN THE CLAIMS:

Amend the claims as follows:

Claim 1-55. (Canceled)

56. (New) An IL-7 drug substance comprising, as the active product, an IL-7 conformer, wherein said conformer comprises the following three disulfide bridges: Cys: 1-4 (Cys2- Cys92); 2-5 (Cys34- Cys129) and 3-6 (Cys47- Cys141), wherein the total amount by weight of IL-7 in said drug substance is at least 98% by weight and wherein said drug substance is substantially free of IL-7 molecular variants or product related impurities.

57. (New) IL-7 drug substance according to claim 56, wherein said IL-7 conformer is a recombinant human IL-7 conformer.

58. (New) IL-7 drug substance according to claim 57, wherein said IL-7 conformer comprises the amino acid sequence of SEQ ID NO: 2 or 4.

59. (New) IL-7 drug substance according to claim 56, wherein said IL-7 conformer is a recombinant simian IL-7 conformer.

60. (New) IL-7 drug substance according to claim 59, wherein said IL-7 conformer comprises the amino acid sequence of SEQ ID NO: 12.

61. (New) IL-7 drug substance according to claim 56, wherein said IL-7 conformer is not glycosylated.

62. (New) IL-7 drug substance according to claim 56, wherein said IL-7 conformer is glycosylated.

63. (New) IL-7 drug substance according to claim 56, wherein said IL-7 conformer is associated to the hepatocyte growth factor as a heterodimer.

64. (New) IL-7 drug substance according to claim 56, wherein said IL-7 conformer is functionally attached to a Fc portion of an IgG heavy chain through a peptide hinge region, said IgG being a human IgG1 or IgG4.

65. (New) IL-7 drug substance according to claim 56, wherein said IL-7 conformer is functionally associated to a Human Serum Albumin (HSA) or a portion of HSA as a fusion protein

66. (New) IL-7 drug substance according to claim 56, said drug substance being substantially free of an other IL-7 conformer.

67. (New) IL-7 drug substance according to claim 56, wherein the total amount by weight of IL-7 in said drug substance is at least 99.5% by weight.

68. (New) A pharmaceutical composition comprising an effective amount of a drug substance according to claim 56 and one or more pharmaceutically acceptable carriers.

69. (New) Pharmaceutical composition according to claim 68, wherein the pharmaceutically acceptable carrier is selected from sucrose, trehalose and an amino acid.

70. (New) Pharmaceutical composition according to claim 69, wherein the pharmaceutically acceptable carrier is contained in an appropriate buffer to form an isotonic solution.

71. (New) Pharmaceutical composition according to claim 70, wherein said appropriate buffer has a pH range comprised between 5 to 7.5.

72. (New) A pharmaceutical composition according to claim 71, wherein said appropriate buffer is an organic salt selected from a sodium citrate buffer and an ammonium acetate buffer.

73. (New) A pharmaceutical composition according to claim 68, wherein said composition is a lyophilized form.

74. (New) A pharmaceutical composition according to claim 68, wherein said composition comprises a protein or a surfactant.

75. (New) A pharmaceutical composition according to claim 68, further comprising an immuno-stimulating agent selected from a hematopoietic cell growth factor, a cytokine, an antigen and an adjuvant, or a combination thereof, for combined, separate or sequential use.

76. (New) A pharmaceutical composition according to claim 75, wherein said hematopoietic cell growth factor is selected from the Stem Cell Factor (SCF), particularly the soluble form of the SCF, G-CSF, GM-CSF, Flt-3 ligand, IL-15 and IL-2.

77. (New) A pharmaceutical composition according to claim 75, wherein the cytokine is selected from γ interferon, IL-2, IL-12, RANTES, B7-1, MIP-2 and MIP-1 α .

78. (New) A pharmaceutical composition according to claim 75, wherein said antigen is selected from a synthetic or natural peptide, a recombinant protein, a killed,

inactivated or attenuated pathogen product, a lipid, a portion thereof and a combination thereof.

79. (New) A pharmaceutical composition according to claim 78, wherein said antigen is selected from antigens derived from HIV, Varicella Zoster virus, Influenza virus, Epstein Barr virus, type I or 2 Herpes Simplex virus, human cytomegalovirus, Dengue virus, Hepatite A, B, C or E virus, Syncytium respiratory virus, human papilloma virus, mycobacterium tuberculosis, Toxoplasma and Chlamydia.

80. (New) A pharmaceutical composition according to claim 75, wherein said adjuvant is selected from any substance, mixture, solute or composition facilitating or increasing the immunogenicity of an antigen and able to induce a Th1-type immune response, such as CpG, QS21, ISCOM and monophosphoryl lipid A.

81. (New) Pharmaceutical composition according to claim 68, for administration to a human patient for prophylactic or therapeutic stimulation of B or T lymphocyte development and proliferation, or for enhancement of global or specific immuno-reconstitution, or for enhancement of humoral or cellular immune response.

82. (New) A pharmaceutical composition according to claim 68, to prevent or reduce opportunistic infections in immunodeficient patients.

83. (New) A pharmaceutical composition according to claim 68, to prolong lymphopoiesis stimulation or to produce specific immune response or to broaden the repertoire of a specific immune response in human patients.

84. (New) A pharmaceutical composition according to claim 81, 82 or 83, wherein human patients are immunodeficient patients, cancer patients, patients undergoing grafts, patients infected with a virus or a parasite, elderly patients or any patients having low CD4 count.

85. (New) A pharmaceutical composition according to claim 68, wherein the effective amount of the drug substance is comprised between about 3 to 300 µg/kg/day, preferably between 10 to 100 µg/kg/day, and in particular administered from once daily, to twice or three times a week down to once weekly.

86. (New) A nucleic acid molecule encoding an IL-7 polypeptide, wherein said nucleic acid molecule comprises an altered Shine-Dalgarno-like sequence.

87. (New) A nucleic acid molecule comprising a sequence selected from SEQ ID Nos: 1, 3, 12, 16, 18, 20 or 22.

88. (New) A vector comprising a nucleic acid according to claim 86.

89. (New) A recombinant host cell comprising a nucleic acid according to claim 87 or a vector containing said nucleic acid.

90. (New) A recombinant host cell according to claim 89, wherein said recombinant host cell is a human cell or a bacterial cell.

91. (New) A recombinant host cell according to claim 90, which is *Escherichia coli* or *Bacillus Brevis*.

92. (New) A recombinant host cell according to claim 90, which is a Chinese Hamster Ovary (CHO), HEK-293 cell line or a human stromal or epithelial cell line.

93. (New) An antibody specifically immunoreactive with an IL-7 conformer as defined in claim 56.

94. (New) A method of producing an IL-7 drug substance as defined in claim 56, the method comprising:

- a) providing a sample comprising IL-7 polypeptides,
- b) purifying an IL-7 conformer which comprises the following three disulfide bridges: Cys: 1-4 (Cys2- Cys92); 2-5 (Cys34- Cys129) and 3-6 (Cys47- Cys141) to produce an IL-7 drug substance, and

c) optionally, measuring or quantifying, in the drug substance, said particular IL-7 conformer.

95. (New) The method of claim 94, wherein said sample is obtained from recombinant prokaryotic or eukaryotic host cells producing IL-7 polypeptides.

96. (New) The method of claim 95, wherein said sample is or derives from a culture of prokaryotic host cells encoding an IL-7 polypeptide and further wherein the method further comprises, prior to step b):

- i) treating said sample to cause a complete denaturation of said IL-7 polypeptides,
- ii) optionally purifying the denatured polypeptide obtained in step i) and
- iii) refolding the polypeptides.

97. (New) The method of claim 96, wherein step i) comprises the dissolution of inclusion bodies in a denaturant buffer.

98. (New) The method of claim 96, wherein step ii) is performed by hydrophobic chromatography, ion-exchange or inverse phase chromatography.

99. (New) The method of claim 97, wherein said hydrophobic chromatography is implemented using HIC butyl.

100. (New) The method of claim 96, wherein step ii) is carried out at a pH comprised between 6 and 9, preferably between 7 and 8,5 inclusive.

101. (New) The method of claim 96, wherein said purification step b) comprises the performance of an affinity chromatography.

102. (New) The method of claim 101, wherein said affinity chromatography is performed on a column of sulfated polysaccharides.

103. (New) The method of claim 102, wherein the sulfated polysaccharide is dextran sulfate or heparin.

104. (New) The method of claim 94, wherein the IL-7 conformer is characterized in the drug substance by Mass spectrometry, infra-red spectroscopy, NMR, by determining circular dichroism, by measuring the affinity toward a specific monoclonal antibody raised against said IL-7 conformer, or heparin affinity chromatography, and measured or quantified by ELISA, bioassay or the affinity of said IL-7 conformer for IL-7 receptor and any method of protein quantification if applied to the isolated conformer.

105. (New) A method of controlling an IL-7-containing preparation, comprising determining the presence and/or relative quantity, in said preparation, of an IL-7 conformer as defined in claim 56.

106. (New) A method of producing an IL-7 drug substance or pharmaceutical composition, said method comprising (i) culturing a recombinant host cell encoding an IL-7 polypeptide, (ii) isolating said recombinant polypeptide to produce an IL-7 drug substance and (iii) optionally, conditioning said IL-7 drug substance to produce a pharmaceutical composition suitable for therapeutic or vaccine use, said method further comprising a step of identifying, characterizing or measuring, in said drug substance or pharmaceutical composition, the quantity and/or quality of an IL-7 conformer as defined in claim 56 and, more preferably, a step of selecting the drug substance or pharmaceutical composition which comprises, as the active ingredient, more than about 98% of said IL-7 conformer.

107. (New) A method according to claim 95, wherein IL-7 expression by the recombinant host cells is inducible, regulated or transient, so that the cell culture and IL-7 expression phases can be dissociated.

108. (New) The method of claim 106, wherein the quantity and/or quality of said IL-7 conformer is determined by mass spectrometry-related methods, with or

without tryptic digest, circular dichroism, NMR, specific monoclonal antibody analysis for disulfide bridges and/or conformation characterization.

109. (New) A method for inducing a prolonged lymphopoiesis stimulation or for amplifying an immune response in a subject, comprising administering to a subject in need thereof an effective amount of an IL-7 drug substance obtained by a method according to claim 94.

110. (New) A method for preventing or treating a disease associated with an immunodeficiency, comprising administering to a subject in need thereof an effective amount of an IL-7 drug substance obtained by a method according to claim 94.